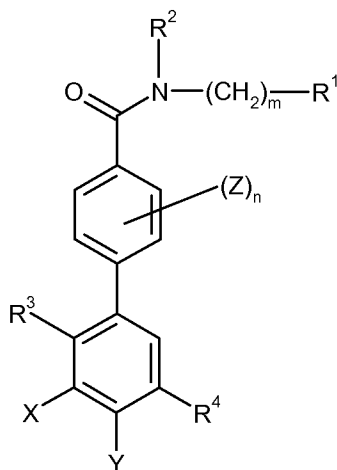


Amendments to the claims

1. (Currently amended) A compound of formula (I):



(I)

wherein

R¹ is selected from hydrogen, C₁₋₆alkyl optionally substituted by up to three groups independently selected from C₁₋₆alkoxy, halogen and hydroxy, C₂₋₆alkenyl, C₃₋₇cycloalkyl optionally substituted by one or more C₁₋₆alkyl groups, phenyl optionally substituted by up to three groups independently selected from R⁵ and R⁶[[, and]]or heteroaryl optionally substituted by up to three groups independently selected from R⁵ and R⁶,

R² is selected from hydrogen, C₁₋₆alkyl [[and]]or -(CH₂)_p-C₃₋₇cycloalkyl optionally substituted by one or more C₁₋₆alkyl groups,

or (CH₂)_mR¹ and R², together with the nitrogen atom to which they are bound, form a four- to six-membered heterocyclic ring optionally substituted by up to three C₁₋₆alkyl groups;

R³ is chloro or methyl;

R⁴ is the group -NH-CO-R⁷ or -CO-NH-(CH₂)_p-R⁸;

R⁵ is selected from C₁₋₆alkyl, C₁₋₆alkoxy, -(CH₂)_p-C₃₋₇cycloalkyl optionally substituted by one or more C₁₋₆alkyl groups, -CONR⁹R¹⁰, -NHCOR¹⁰,

-SO₂NHR⁹, -(CH₂)_qNHSO₂R¹⁰, halogen, CN, OH, -(CH₂)_qNR¹¹R¹² [[, and]]_or trifluoromethyl;

R⁶ is selected from C₁₋₆alkyl, C₁₋₆alkoxy, halogen, trifluoromethyl [[and]]_or -(CH₂)_qNR¹¹R¹²;

R⁷ is selected from hydrogen, C₁₋₆alkyl, -(CH₂)_p-C₃₋₇cycloalkyl optionally substituted by one or more C₁₋₆alkyl groups, trifluoromethyl, -(CH₂)_rheteroaryl optionally substituted by R¹³ and/or R¹⁴[[, and]]_or -(CH₂)_rphenyl optionally substituted by R¹³ and/or R¹⁴;

R⁸ is selected from hydrogen, C₁₋₆alkyl, C₃₋₇cycloalkyl optionally substituted by one or more C₁₋₆alkyl groups, CONHR⁹, phenyl optionally substituted by R¹³ and/or R¹⁴ [[, and]]_or heteroaryl optionally substituted by R¹³ and/or R¹⁴;

R⁹ and R¹⁰ are each independently selected from hydrogen [[and]]_or C₁₋₆alkyl, or

R⁹ and R¹⁰, together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R¹⁵, wherein the ring is optionally substituted by up to two C₁₋₆alkyl groups;

R¹¹ is selected from hydrogen, C₁₋₆alkyl [[and]]_or -(CH₂)_p-C₃₋₇cycloalkyl optionally substituted by one or more C₁₋₆alkyl groups [[,]] ;

R¹² is selected from hydrogen [[and]]_or C₁₋₆alkyl, or

R¹¹ and R¹², together with the nitrogen atom to which they are bound, form a five or six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R¹⁵;

R¹³ is selected from C₁₋₆alkyl, C₁₋₆alkoxy, -(CH₂)_p-C₃₋₇cycloalkyl optionally substituted by one or more C₁₋₆alkyl groups, -CONR⁹R¹⁰, -NHCOR¹⁰, halogen, CN, -(CH₂)_qNR¹¹R¹², trifluoromethyl, phenyl optionally substituted by one or more R¹⁴ groups [[and]]_or heteroaryl optionally substituted by one or more R¹⁴ groups;

R¹⁴ is selected from C₁₋₆alkyl, C₁₋₆alkoxy, halogen, trifluoromethyl [[and]]_or -NR¹¹R¹²;

R¹⁵ is selected from hydrogen [[and]]_or methyl;

X and Y are each independently selected from hydrogen, methyl [[and]]_or halogen;

Z is selected from $-(\text{CH}_2)_s\text{OR}^{16}$, $-(\text{CH}_2)_s\text{NR}^{16}\text{R}^{17}$, $-(\text{CH}_2)_s\text{CH}_2\text{CH}_2\text{R}^{16}$, $-(\text{CH}_2)_s\text{COOR}^{16}$, $-(\text{CH}_2)_s\text{CONR}^{16}\text{R}^{17}$, $[-(\text{CH}_2)_s\text{NHCOR}^{16}]$, $-(\text{CH}_2)_s\text{NHCONR}^{16}\text{R}^{17}$, $-(\text{CH}_2)_s\text{SO}_2\text{R}^{16}$, $-(\text{CH}_2)_s\text{SO}_2\text{NR}^{16}\text{R}^{17}$ or $-(\text{CH}_2)_s\text{NHSO}_2\text{R}^{16}$;

R^{16} is selected from hydrogen, C_{1-6} alkyl optionally substituted by up to two hydroxy groups, $-(\text{CH}_2)_t\text{OR}^{18}$, $-(\text{CH}_2)_t\text{NR}^{18}\text{R}^{19}$, $-(\text{CH}_2)_t\text{NHSO}_2\text{R}^{18}$, $-(\text{CH}_2)_t\text{CONR}^{18}\text{R}^{19}$, $-(\text{CH}_2)_t\text{COOR}^{18}$, $-(\text{CH}_2)_t$ heteroaryl optionally substituted by up to two groups independently selected from halogen, C_{1-6} alkyl or oxo, or $-(\text{CH}_2)_t$ phenyl optionally substituted by up to two groups independently selected from halogen, C_{1-6} alkyl or C_{1-6} alkoxy,

R^{17} is selected from hydrogen or C_{1-6} alkyl, or

R^{16} and R^{17} , together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R^{15} , wherein the ring is optionally substituted by up to two groups independently selected from oxo, halogen or C_{1-6} alkyl;

R^{18} and R^{19} are each independently selected from hydrogen or C_{1-6} alkyl optionally substituted by up to two hydroxy groups, or

R^{18} and R^{19} , together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R^{15} , wherein the ring is optionally substituted by up to two groups independently selected from oxo, halogen or C_{1-6} alkyl;

m is selected from 0, 1, 2, 3 or 4, wherein each carbon atom of the resulting carbon chain may be optionally substituted with up to two groups independently selected from C_{1-6} alkyl or halogen;

n is 1;

p is selected from 0, 1 or 2;

q is selected from 0, 1, 2 or 3;

r is selected from 0 or 1;

s is selected from 0, 1, 2, 3 and 4; and

t is selected from 1, 2, 3 or 4;

or a pharmaceutically acceptable salt thereof.

2. (currently amended) A compound according to claim 1 wherein R^1 is selected from C_{1-6} alkyl, C_{3-7} cycloalkyl ~~[[and]]~~ or phenyl optionally substituted by up to three groups selected from R^5 and R^6 .

3. (previously presented) A compound according to claim 1 wherein R^1 is C_{3-6} cycloalkyl.

4. (previously presented) A compound according to claim 1 wherein R^2 is hydrogen.

5. (previously presented) A compound according to claim 1 wherein m is 0 or 1.

6. (previously presented) A compound according to claim 1 wherein m is 1.

7. (previously presented) A compound according to claim 1 wherein R^8 is C_{3-6} cycloalkyl.

8. (Currently amended) A compound according to claim 1 wherein Z is selected from $-(CH_2)_8OR^{16}$, $-(CH_2)_8NR^{16}R^{17}$, $[-(CH_2)_8NHCOR^{16}]$, $-(CH_2)_8NHCONR^{16}R^{17}$ and $-(CH_2)_8NHSO_2R^{16}$.

9. (Currently amended) A compound according to claim 1 ~~substantially as hereinbefore defined with reference to any one of Examples 1 to 48,~~

N^3 -cyclopropyl-5-fluoro-2'-hydroxy-6-methyl- $N^{4'}$ -[(4-methylphenyl)methyl]-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl- $N^{4'}$ -(2,2-dimethylpropyl)-5-fluoro-6-methyl-2'-{[(methyloxy)methyl]oxy}-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl-5-fluoro-6-methyl-2'-{[(methyloxy)methyl]oxy}- $N^{4'}$ -(2-methylpropyl)-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl- $N^{4'}$ -(cyclopropylmethyl)-5-fluoro-6-methyl-2'-{[(methyloxy)methyl]oxy}-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl-5-fluoro-6-methyl-2'-{[(methyloxy)methyl]oxy}- N^{4i} -{[4-(methyloxy)phenyl]methyl}-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl-5-fluoro-6-methyl-2'-{[(methyloxy)methyl]oxy}- N^{4i} -[(1*R*)-1,2,2-trimethylpropyl]-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl- N^{4i} -[(1*R*)-1,2-dimethylpropyl]-5-fluoro-6-methyl-2'-{[(methyloxy)methyl]oxy}-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl- N^{4i} -(2,2-dimethylpropyl)-5-fluoro-2'-hydroxy-6-methyl-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl-5-fluoro-2'-hydroxy-6-methyl- N^{4i} -(2-methylpropyl)-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl- N^{4i} -(cyclopropylmethyl)-5-fluoro-2'-hydroxy-6-methyl-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl-5-fluoro-2'-hydroxy-6-methyl- N^{4i} -{[4-(methyloxy)phenyl]methyl}-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl-5-fluoro-2'-hydroxy-6-methyl- N^{4i} -[(1*R*)-1,2,2-trimethylpropyl]-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl- N^{4i} -[(1*R*)-1,2-dimethylpropyl]-5-fluoro-2'-hydroxy-6-methyl-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl- N^{4i} -(2,2-dimethylpropyl)-5-fluoro-6-methyl-2'-(methyloxy)-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl-5-fluoro-6-methyl-2'-(methyloxy)- N^{4i} -(2-methylpropyl)-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl- N^{4i} -(cyclopropylmethyl)-5-fluoro-6-methyl-2'-(methyloxy)-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl-5-fluoro-6-methyl-2'-(methyloxy)- N^{4i} -{[4-(methyloxy)phenyl]methyl}-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl-5-fluoro-6-methyl-2'-(methyloxy)- N^{4i} -[(1*R*)-1,2,2-trimethylpropyl]-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl- N^{4i} -[(1*R*)-1,2-dimethylpropyl]-5-fluoro-6-methyl-2'-(methyloxy)-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl- N^{4i} -(2,2-dimethylpropyl)-5-fluoro-6-methyl-2'-(propyloxy)-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl-2'-{[3-(dimethylamino)propyl]oxy}- N^{4i} -(2,2-dimethylpropyl)-5-fluoro-6-methyl-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl- N^{4i} -(2,2-dimethylpropyl)-5-fluoro-6-methyl-2'-({2-[(methylsulfonyl)amino]ethyl}oxy)-3,4'-biphenyldicarboxamide;

4-[(5'-[(cyclopropylamino)carbonyl]-4-{[(2,2-dimethylpropyl)amino]carbonyl}-3'-fluoro-2'-methyl-2-biphenyl)oxy]butanoic acid;

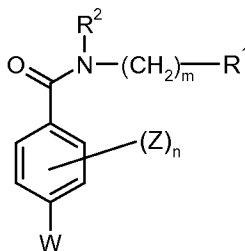
2'-[(4-amino-4-oxobutyl)oxy]- N^3 -cyclopropyl- N^{4i} -(2,2-dimethylpropyl)-5-fluoro-6-methyl-3,4'-biphenyldicarboxamide;

N^3 -cyclopropyl- N^{4i} -(2,2-dimethylpropyl)-5-fluoro-6-methyl-2'-{[4-(methylamino)-4-oxobutyl]oxy}-3,4'-biphenyldicarboxamide;

*N*³-cyclopropyl-*N*⁴-(2,2-dimethylpropyl)-5-fluoro-2'-[(4-hydroxybutyl)oxy]-6-methyl-3,4'-biphenyldicarboxamide;
*N*³-cyclopropyl-*N*⁴-(2,2-dimethylpropyl)-5-fluoro-6-methyl-2'-{[3-(1,3,4-oxadiazol-2-yl)propyl]oxy}-3,4'-biphenyldicarboxamide; and
*N*³-cyclopropyl-*N*⁴-(2,2-dimethylpropyl)-5-fluoro-2'-(hydroxymethyl)-6-methyl-3,4'-biphenyldicarboxamide;
or a pharmaceutically acceptable [[derivative]] salt thereof.

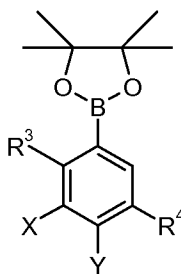
10. (previously presented) A process for preparing a compound according to claim 1, or a pharmaceutically acceptable [[derivative]] salt thereof, which comprises:

(a) reacting a compound of (II)



(II)

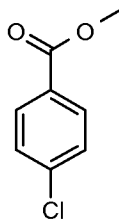
in which R¹, R², Z, m and n are as defined in claim 1 and W is halogen, with a compound of formula (III)



(III)

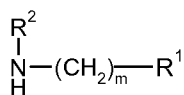
in which R³, R⁴, X and Y are as defined in claim 1, in the presence of a catalyst, or

(b) reacting a compound of formula (VIII)



(VIII)

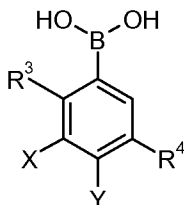
with a compound of formula (III) as hereinbefore defined and then reacting the acid thus formed with an amine of formula (V)



(V)

in which R¹, R² and m are as defined in claim 1,
 under amide forming conditions

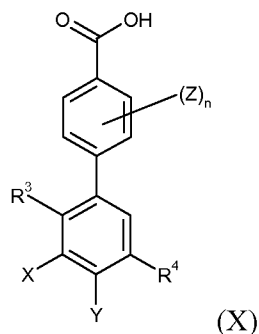
(c) reacting a compound of formula (II) as hereinbefore defined with a compound of formula (IX)



(IX)

in which R³, R⁴, X and Y are as defined in claim 1,
 in the presence of a catalyst,

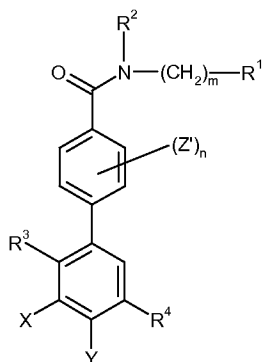
(d) reacting a compound of formula (X)



in which R^3 , R^4 , X, Y, Z and n are as defined in claim 1,
 with an amine compound of formula (V) as defined above,
 under amide forming conditions,

(e) final stage modification of one compound of formula (I) into another compound of formula (I), or

(f) conversion of a compound of formula (XII)



(XII)

in which Z' is a group convertible to Z as defined in claim 1.

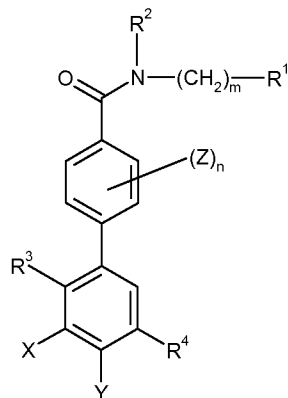
11. (currently amended) A pharmaceutical composition comprising at least one compound according to claim 1, or a pharmaceutically acceptable salt [[derivative]] thereof, in association with one or more pharmaceutically acceptable excipients, diluents and/or carriers.

12. (currently amended) A method for treating inflammation in a human in need thereof ~~a condition or disease state mediated by p38 kinase activity or mediated by~~

~~cytokines produced by the activity of p38 kinase comprising administering to said human an effective amount of a patient in need thereof~~ a compound according to claim 1, or a pharmaceutically acceptable [[derivative]] salt thereof.

13. - 14. (cancelled)

15. (currently amended) A compound of formula (IA):



(IA)

wherein

R¹ is selected from hydrogen, C₁₋₆alkyl optionally substituted by up to three groups independently selected from C₁₋₆alkoxy, halogen or hydroxy, C₂₋₆alkenyl, C₃₋₇cycloalkyl optionally substituted by one or more C₁₋₆alkyl groups, phenyl optionally substituted by up to three groups independently selected from R⁵ and R⁶, or heteroaryl optionally substituted by up to three groups independently selected from R⁵ and R⁶,

R² is selected from hydrogen, C₁₋₆alkyl or -(CH₂)_p-C₃₋₇cycloalkyl optionally substituted by one or more C₁₋₆alkyl groups,

or (CH₂)_mR¹ and R², together with the nitrogen atom to which they are bound, form a four- to six-membered heterocyclic ring optionally substituted by up to three C₁₋₆alkyl groups;

R³ is chloro or methyl;

R⁴ is the group -NH-CO-R⁷ or -CO-NH-(CH₂)_p-R⁸;

R⁵ is selected from C₁₋₆alkyl, C₁₋₆alkoxy, -(CH₂)_p-C₃₋₇cycloalkyl optionally substituted by one or more C₁₋₆alkyl groups, -CONR⁹R¹⁰, -NHCOR¹⁰, -SO₂NHR⁹, -(CH₂)_qNHSO₂R¹⁰, halogen, CN, OH, -(CH₂)_qNR¹¹R¹² or trifluoromethyl;

R^6 is selected from C_{1-6} alkyl, C_{1-6} alkoxy, halogen, trifluoromethyl [[and]] or $-(CH_2)_qNR^{11}R^{12}$;

R^7 is selected from hydrogen, C_{1-6} alkyl, $-(CH_2)_pC_{3-7}$ cycloalkyl optionally substituted by one or more C_{1-6} alkyl groups, trifluoromethyl, $-(CH_2)_r$ heteroaryl optionally substituted by R^{13} and/or R^{14} [[, and]] or $-(CH_2)_r$ phenyl optionally substituted by R^{13} and/or R^{14} ;

R^8 is selected from hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl optionally substituted by one or more C_{1-6} alkyl groups, $CONHR^9$, phenyl optionally substituted by R^{13} and/or R^{14} [[, and]] or heteroaryl optionally substituted by R^{13} and/or R^{14} ;

R^9 and R^{10} are each independently selected from hydrogen [[and]] or C_{1-6} alkyl, or

R^9 and R^{10} , together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N- R^{15} , wherein the ring is optionally substituted by up to two C_{1-6} alkyl groups;

R^{11} is selected from hydrogen, C_{1-6} alkyl [[and]] or $-(CH_2)_pC_{3-7}$ cycloalkyl optionally substituted by one or more C_{1-6} alkyl groups,

R^{12} is selected from hydrogen [[and]] or C_{1-6} alkyl, or

R^{11} and R^{12} , together with the nitrogen atom to which they are bound, form a five or six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N- R^{15} ;

R^{13} is selected from C_{1-6} alkyl, C_{1-6} alkoxy, $-(CH_2)_pC_{3-7}$ cycloalkyl optionally substituted by one or more C_{1-6} alkyl groups, $-CONR^9R^{10}$, $-NHCOR^{10}$, halogen, CN, $-(CH_2)_qNR^{11}R^{12}$, trifluoromethyl, phenyl optionally substituted by one or more R^{14} groups [[and]] or heteroaryl optionally substituted by one or more R^{14} groups;

R^{14} is selected from C_{1-6} alkyl, C_{1-6} alkoxy, halogen, trifluoromethyl [[and]] or $-NR^{11}R^{12}$;

R^{15} is selected from hydrogen [[and]] or methyl;

X and Y are each independently selected from hydrogen, methyl [[and]] or halogen;

Z is selected from $-(CH_2)_sOR^{16}$, $-(CH_2)_sNR^{16}R^{17}$, $-(CH_2)_sCH_2CH_2R^{16}$, $-(CH_2)_sCOOR^{16}$, $-(CH_2)_sCONR^{16}R^{17}$, $-(CH_2)_sNHCOR^{16}$,

$-(\text{CH}_2)_s\text{NHCONR}^{16}\text{R}^{17}$, $-(\text{CH}_2)_s\text{SO}_2\text{R}^{16}$, $-(\text{CH}_2)_s\text{SO}_2\text{NR}^{16}\text{R}^{17}$ [[and]] or
 $-(\text{CH}_2)_s\text{NHSO}_2\text{R}^{16}$;

R^{16} is selected from hydrogen, C_{1-6} alkyl, $-(\text{CH}_2)_t\text{OR}^{18}$, $-(\text{CH}_2)_t\text{NR}^{18}\text{R}^{19}$,
 $-(\text{CH}_2)_t\text{COOR}^{18}$, $-(\text{CH}_2)_t$ heteroaryl optionally substituted by up to two groups
independently selected from halogen [[and]] or C_{1-6} alkyl, [[and]] or is a $-(\text{CH}_2)_t$ phenyl
optionally substituted by up to two groups independently selected from halogen,
 C_{1-6} alkyl [[and]] or C_{1-6} alkoxy,

R^{17} is selected from hydrogen [[and]] or C_{1-6} alkyl, or

R^{16} and R^{17} , together with the nitrogen atom to which they are bound, form
a five- to six-membered heterocyclic ring optionally containing one additional
heteroatom selected from oxygen, sulfur and N-R^{15} , wherein the ring is optionally
substituted by up to two groups independently selected from oxo, halogen and
 C_{1-6} alkyl;

R^{18} and R^{19} are each independently selected from hydrogen [[and]] or
 C_{1-6} alkyl, or

R^{18} and R^{19} , together with the nitrogen atom to which they are bound, form
a five- to six-membered heterocyclic ring optionally containing one additional
heteroatom selected from oxygen, sulfur and N-R^{15} , wherein the ring is optionally
substituted by up to two groups independently selected from oxo, halogen [[and]] or
 C_{1-6} alkyl;

m is selected from 0, 1, 2, 3 [[and]] or 4, wherein each carbon atom of the
resulting carbon chain may be optionally substituted with up to two groups
independently selected from C_{1-6} alkyl [[and]] or halogen;

n is 1;

p is selected from 0, 1 [[and]] or 2;

q is selected from 0, 1, 2 [[and]] or 3;

r is selected from 0 [[and]] or 1;

s is selected from 0, 1, 2, 3 [[and]] or 4; and

t is selected from 2, 3 [[and]] or 4;

or a pharmaceutically acceptable [[derivative]] salt thereof.

USSN: 10/551,502

Art Unit: 1626

16. (new) A pharmaceutical composition comprising a compound according to claim 15, or a pharmaceutically salt thereof, in association with one or more pharmaceutically acceptable excipients, diluents and/or carriers.

17. (new) The compound according to claim 1 which is:

*N*³-Cyclopropyl-*N*⁴-(2,2-dimethylpropyl)-5-fluoro-2'-(hydroxymethyl)-6-methyl-3,4'-biphenyldicarboxamide, or a pharmaceutically acceptable salt thereof.